



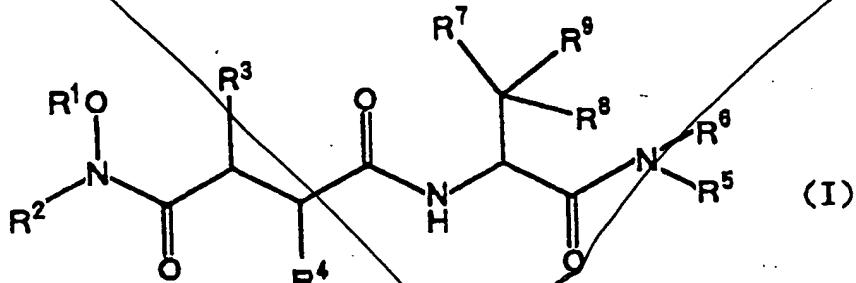
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In the Claims:

Kindly cancel claim 1 without prejudice.

Please amend the claims as follows:

2. (Amended) A compound having the following formula (I):



wherein

$\text{R}^1$  and  $\text{R}^2$  are hydrogen;

$\text{R}^3$  is selected from the group consisting of ( $\text{C}_1\text{-C}_9$ ) alkyl, ( $\text{C}_3\text{-C}_7$ ) cycloalkyl-substituted lower ( $\text{C}_1\text{-C}_4$ ) alkyl, amino-substituted ( $\text{C}_1\text{-C}_6$ ) alkyl, phenyl-lower ( $\text{C}_1\text{-C}_4$ ) alkyl, guanido-substituted phenyl-lower ( $\text{C}_1\text{-C}_4$ ) alkyl, amino-substituted phenyl-lower ( $\text{C}_1\text{-C}_4$ ) alkyl, carboxy-substituted phenyl-lower ( $\text{C}_1\text{-C}_4$ ) alkyl, carbamoyl-substituted phenyl-lower ( $\text{C}_1\text{-C}_4$ ) alkyl, hydroxy-substituted phenyl-lower ( $\text{C}_1\text{-C}_4$ ) alkyl, guanido-substituted lower ( $\text{C}_1\text{-C}_4$ ) alkyl-substituted phenyl-lower ( $\text{C}_1\text{-C}_4$ ) alkyl, unprotected or optionally protected

amino-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, hydroxy-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, lower ( $C_1-C_4$ ) alkoxy carbonyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, lower ( $C_1-C_4$ ) alkylimino-substituted ( $C_1-C_6$ ) alkyl, lower ( $C_1-C_4$ ) acylimidoylimino-substituted ( $C_1-C_6$ ) alkyl, arylmethylimino-substituted ( $C_1-C_6$ ) alkyl, nitrogen-containing heterocyclic radical-substituted lower ( $C_1-C_4$ ) alkylimino-substituted ( $C_1-C_6$ ) alkyl, nitrogen-containing heterocyclic radical-substituted lower ( $C_1-C_4$ ) alkyl, oxygen-containing ( $C_1-C_8$ ) straight chain or branched alkyl, arylsulfonamido-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, alkylsulfonamido-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, aryloxy-substituted lower ( $C_1-C_4$ ) alkyl, and hydroxy-substituted ( $C_1-C_8$ ) alkyl;

$R^4$  is selected from the group consisting of ( $C_3-C_9$ ) alkyl, hydroxy-substituted ( $C_3-C_8$ ) alkyl, and unsubstituted or optionally substituted aryl-lower ( $C_1-C_4$ ) alkyl;

$R^5$  is selected from the group consisting of lower ( $C_1-C_4$ ) alkyl, ( $C_3-C_7$ ) cycloalkyl, mono- or di-lower ( $C_1-C_4$ ) alkylamino-substituted lower ( $C_1-C_4$ ) alkyl, carboxy-substituted lower ( $C_1-C_4$ ) alkyl, hydroxy-substituted ( $C_1-C_6$ ) alkyl, bis(phosphono)-hydroxymethyl-substituted ( $C_1-C_{11}$ ) alkyl, tetrabenzyl bis(phosphono)hydroxymethyl-substituted ( $C_1-C_{11}$ ) alkyl, and a nitrogen-containing heterocyclic radical;

$R^6$  is hydrogen;

$R^7$  is hydrogen or lower ( $C_1-C_4$ ) alkyl;

$R^8$  is hydrogen or lower ( $C_1-C_4$ ) alkyl; and

$R^9$  is selected from the group consisting of hydrogen, hydroxy, amino, and a group of the formula:  $-X-Y$  wherein  $X$  is ( $C_1-C_6$ ) alkylene or phenylene, and

$Y$  is a group of the formula:  $-A-B$  or  $-B$

wherein  $B$  is selected from the group consisting of hydrogen, amino, amidino, lower ( $C_1-C_4$ ) acylimidoyl, unsubstituted or

optionally substituted benzimidoyl, bis(phosphono)methyl, tetra-lower ( $C_1-C_4$ ) alkyl bis(phosphono)methyl, tri-lower ( $C_1-C_4$ ) alkyl bis(phosphono)methyl, bis(phosphono)hydroxymethyl, tetrabenzyl bis(phosphono)hydroxymethyl, and lower ( $C_1-C_4$ ) alkyl-substituted imidazol-3-yl, and

$A$  is selected from the group consisting of lower ( $C_1-C_4$ ) alkylene, imino, and lower ( $C_1-C_4$ ) alkylene-imino;

provided that a combination wherein  $R^7$  is methyl,  $R^8$  is methyl and  $R^9$  is methyl is excluded;

or a pharmaceutically acceptable salt or solvate thereof.

2. (Amended) The compound according to claim 2, wherein

$R^1$  and  $R^2$  are hydrogen;

$R^3$  is selected from the group consisting of methyl, isobutyl, aminopropyl, phenylpropyl, guanidophenylpropyl, aminophenylpropyl, hydroxyphenylpropyl, carboxyphenylpropyl, carbamoylphenylpropyl, aminomethylphenylpropyl, guanidomethylphenylpropyl, hydroxymethylphenylpropyl, aminomethylbenzyl, toluenesulfonamido-methylbenzyl, methanesulfonamido-methylbenzyl, isobutyliminomethylbenzyl, phthalimidomethylbenzyl, phenoxyethyl, aminopentyl, acetimidoyliminopentyl, isobutyliminopentyl, pyridylmethylimino-pentyl, methoxycarbonylphenylpropyl, ethoxyethoxyethyl, hydroxyoctyl, butoxyethyl, iso-butoxyethyl, morpholinopropyl, (3,4,4-trimethyl-2,5-dioxo-imidazolidin-1-yl)propyl, cyclohexylpropyl, and piperidinopropyl;

$R^4$  is selected from the group consisting of naphthylmethyl, phenylpropyl, isobutyl, tert-butyl, isopropyl, and hydroxyoctyl;

$R^5$  is selected from the group consisting of methyl, cyclopropyl, 2-(*N,N*-dimethylamino)ethyl, 2-carboxyethyl, 2-hydroxyethyl, 2-hydroxy-1,1-dimethylethyl, 2-hydroxy-1-methylethyl, 6,6-bis(phosphono)-6-hydroxyhexyl, tetrabenzyl 6,6-bis(phosphono)-6-hydroxyhexyl, piperidyl, and morpholinyl;

$R^6$  is hydrogen;

$R^7$  is hydrogen or methyl;

$R^8$  is hydrogen or methyl; and

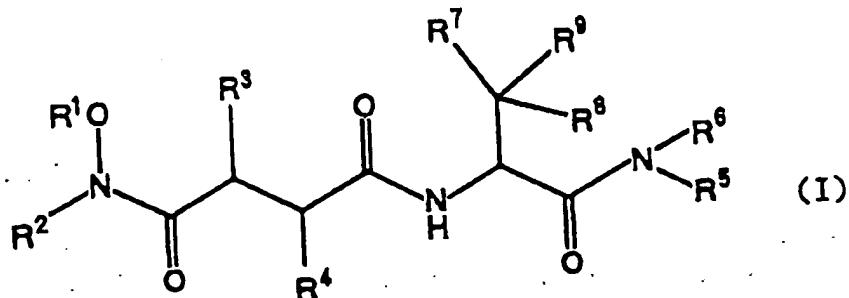
~~R<sup>9</sup> is selected from the group consisting of hydrogen, hydroxy, amino, and a group of the formula: -X-Y wherein X is selected from the group consisting of methylene, ethylene, trimethylene, tetramethylene, pentamethylene, hexamethylene, and phenylene, and~~

~~Y is a group of the formula: -A-B or -B wherein B is selected from the group consisting of amino, amidino, acetimidoyl, propionimidoyl, benzimidoyl, bis(phosphono)methyl, tetraethyl bis(phosphono)methyl, triethyl bis(phosphono)methyl, tetramethyl bis(phosphono)methyl, trimethyl bis(phosphono)methyl, bis(phosphono)-hydroxymethyl, tetrabenzyl bis(phosphono)hydroxymethyl, and 2-methyl-imidazol-3-yl, and~~

~~A is selected from the group consisting of imino, methyleneimino, and methylene.~~

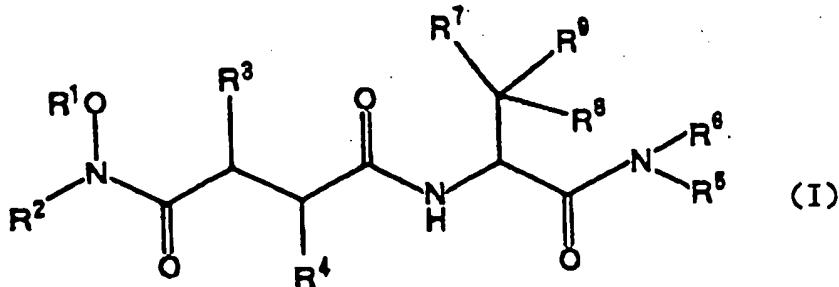
*(Twice Amended)*

4. ~~(Amended)~~ A pharmaceutical or veterinary composition which comprises (a) an effective amount of at least a member selected from the group consisting of a compound of the formula (I):



wherein R<sup>1</sup> to R<sup>9</sup>, all have the same meanings as defined in claim 10, and a pharmaceutically or veterinarily acceptable salt or solvate thereof, and (b) a pharmaceutically or veterinarily acceptable excipient or carrier.

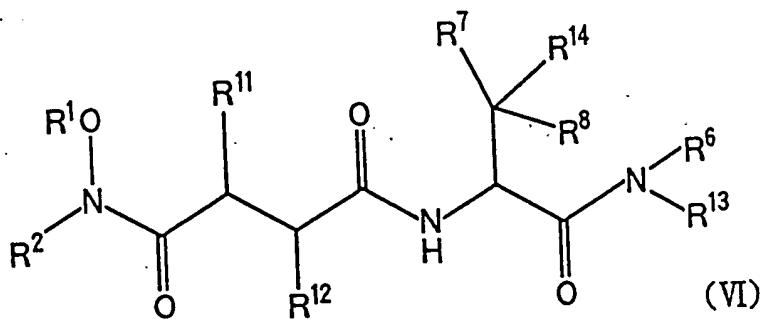
5. (Twice Amended) (Amended) A metalloproteinase inhibitor which comprises an effective amount of at least a member selected from the group consisting of a compound of the formula (I):



wherein R<sup>1</sup> to R<sup>9</sup>, all have the same meanings as defined in claim 2, and a pharmaceutically acceptable salt or solvate thereof.

8. (Twice Amended) (Amended) A method of prophylactically and/or therapeutically treating diseases and/or disorders associated with tissue degradation comprising administering an effective amount of the compound according to claim 2.

12. (Twice Amended) (Amended) A compound having the following formula (VI):



wherein R<sup>1</sup>, R<sup>2</sup>, and R<sup>6</sup> to R<sup>8</sup>, all have the same meanings as defined in claim 2.

$R^{11}$  has the same meaning as defined for  $R^3$ , or is selected from the group consisting of protected hydroxy, protected guanido-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected amino-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, nitro-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected amino-substituted ( $C_1-C_6$ ) alkyl, nitro-substituted ( $C_1-C_6$ ) alkyl, protected carboxy-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected hydroxy-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected guanido-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected amino-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected hydroxy-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected carboxy-substituted lower ( $C_1-C_4$ ) alkyl, protected hydroxy-alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected hydroxy-containing ( $C_1-C_8$ ) straight chain or branched alkyl, and cyano-substituted phenyl-lower ( $C_1-C_4$ ) alkyl;

$R^{12}$  has the same meaning as defined for  $R^4$ , or is protected hydroxy-substituted ( $C_1-C_8$ ) alkyl;

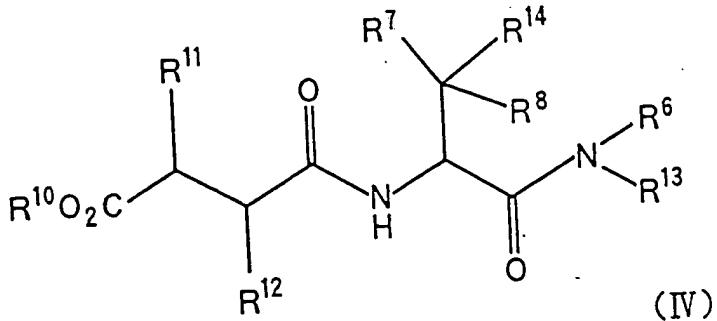
$R^{13}$  has the same meaning as defined for  $R^5$ , or is selected from the group consisting of protected carboxy-substituted lower ( $C_1-C_4$ ) alkyl, protected hydroxy-substituted lower ( $C_1-C_4$ ) alkyl, protected bis(phosphono)hydroxymethyl-substituted ( $C_1-C_{11}$ ) alkyl, and a protected nitrogen-containing heterocyclic group; and

$R^{14}$  has the same meaning as defined for  $R^9$ , or is selected from the group consisting of protected amino, protected hydroxy, and a group of the formula:  $-X-E$  or  $-X-A-E$

wherein X and A, both have the same meanings as given above, and E is selected from the group consisting of nitro, cyano, amino, carboxyl, ( $C_1-C_{11}$ ) hydroxyalkyl, protected amino, protected guanido, protected amidino, protected acylimidoyl, protected benzimidoyl, protected bis(phosphono)methyl, protected bis(phosphono)hydroxymethyl, and protected ( $C_1-C_{11}$ ) alkyl-substituted imidazol-3-yl;

or a salt thereof.

13. (Twice Amended) <sup>(Amended)</sup> A compound having the following formula (IV):



wherein R<sup>6</sup> to R<sup>8</sup>, all have the same meanings as defined in claim

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R<sup>10</sup> is selected from the group consisting of unsubstituted or optionally substituted alkyl, unsubstituted or optionally substituted aralkyl, and a carboxy-protecting group;

R<sup>11</sup> has the same meaning as defined for R<sup>3</sup>, or is selected from the group consisting of protected hydroxy, protected guanido-substituted phenyl-lower (C<sub>1</sub>-C<sub>4</sub>) alkyl, protected amino-substituted phenyl-lower (C<sub>1</sub>-C<sub>4</sub>) alkyl, nitro-substituted phenyl-lower (C<sub>1</sub>-C<sub>4</sub>) alkyl, protected amino-substituted (C<sub>1</sub>-C<sub>6</sub>) alkyl, nitro-substituted (C<sub>1</sub>-C<sub>6</sub>) alkyl, protected carboxy-substituted phenyl-lower (C<sub>1</sub>-C<sub>4</sub>) alkyl, protected hydroxy-substituted phenyl-lower (C<sub>1</sub>-C<sub>4</sub>) alkyl, protected guanido-substituted lower (C<sub>1</sub>-C<sub>4</sub>) alkyl-substituted phenyl-lower (C<sub>1</sub>-C<sub>4</sub>) alkyl, protected amino-substituted lower (C<sub>1</sub>-C<sub>4</sub>) alkyl-substituted phenyl-lower (C<sub>1</sub>-C<sub>4</sub>) alkyl, protected hydroxy-substituted lower (C<sub>1</sub>-C<sub>4</sub>) alkyl-substituted phenyl-lower (C<sub>1</sub>-C<sub>4</sub>) alkyl, protected carboxy-substituted lower (C<sub>1</sub>-C<sub>4</sub>) alkyl-substituted phenyl-lower (C<sub>1</sub>-C<sub>4</sub>) alkyl, protected hydroxy-containing (C<sub>1</sub>-C<sub>8</sub>) straight chain or branched alkyl, and cyano-substituted phenyl-lower (C<sub>1</sub>-C<sub>4</sub>) alkyl;

R<sup>12</sup> has the same meaning as defined for R<sup>4</sup>, or is protected hydroxy-substituted (C<sub>1</sub>-C<sub>8</sub>) alkyl;

bis(phosphono)methyl, protected bis(phosphono)hydroxymethyl, and protected ( $C_1$ - $C_{11}$ ) alkyl-substituted imidazol-3-yl;

$R^{13}$  has the same meaning as defined for  $R^5$ , or is selected from the group consisting of protected carboxy-substituted lower ( $C_1$ - $C_4$ ) alkyl, protected hydroxy-substituted lower ( $C_1$ - $C_4$ ) alkyl, protected bis(phosphono)hydroxymethyl-substituted ( $C_1$ - $C_{11}$ ) alkyl, and a protected nitrogen-containing heterocyclic group; and

$R^{14}$  has the same meaning as defined for  $R^9$ , or is selected from the group consisting of protected amino, protected hydroxy, and a group of the formula:  $-X-E$  or  $-X-A-E$  wherein X and A, both have the same meanings as given above, and E is selected from the group consisting of nitro, cyano, amino, carboxyl, ( $C_1$ - $C_{11}$ ) hydroxyalkyl, protected amino, protected guanido, protected amidino, protected acylimidoyl, protected benzimidoyl, protected

or a salt thereof.